Familial Polycythemia Vera in Father and Daughter

To the Editor: Polycythemia vera (PV) is a chronic myeloproliferative disorder which usually affects the elderly. We report a familial case of PV involving a father and daughter; the latter patient was diagnosed at the relatively young age of 24 years. Human leukocyte antigen (HLA) typing revealed a possible HLA haplotype associated with familial PV.

Patient 1

A 57-year-old Japanese man was admitted to our hospital because of a headache in December, 1989. Laboratory findings on admission were as follows: red blood cells (RBC) 7.14×10^{12}/l, hemoglobin 16.1 g/dl, platelets, $1{,}359 \times 10^{9}$/l, and white blood cells (WBC) 20×10^{9}/l. Leukocyte alkaline phosphatase (LAP) score was elevated at 372 (normal range: 170–285). Bone marrow showed normocellularity with normal differentiation counts. Cytogenetic study demonstrated 46XY. RBC volume was 38.7 ml/kg (normal range: 25–35 ml/kg), and the arterial oxygen saturation (SaO_2) did not suggest hypoxemia. Serum vitamin B_{12} and erythropoietin concentrations were 711 pg/ml (normal range: 230–800 pg/ml) and 6.8 mU/ml (normal range: 8–36 mU/ml), respectively. Mild splenomegaly was observed. From these findings, he was diagnosed with PV. He has been treated with ranimustine (50–100 mg/body weight, intravenously, every fourth month) with neither any side effects nor observable symptoms due to PV.

Patient 2

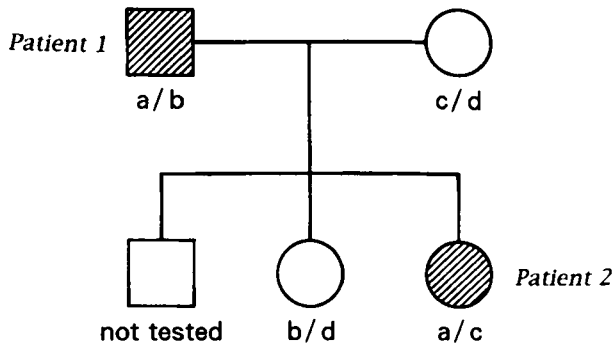
A 24-year-old Japanese woman, the daughter of patient 1, demonstrated abnormal blood counts on a routine screening examination in October, 1991. Laboratory findings at that time were as follows: RBC 8.45×10^{12}/l, hemoglobin 20.5 g/dl, platelets 741×10^{9}/l, and WBC 10×10^{9}/l. LAP score was elevated at 387. Bone marrow showed normocellularity with normal differentiation counts. Cytogenetic study demonstrated 46XX. RBC volume was 59.0 ml/kg, and SaO_2 did not suggest hypoxemia. Serum vitamin B_{12} and erythropoietin concentrations were 759 pg/ml and 6.8 mU/ml, respectively. Mild splenomegaly was observed. From these findings, the patient was diagnosed with PV. She has been treated with phlebotomy without severe symptoms.

Discussion

Figure 1 shows the results of HLA typings performed on this family. Among these family members, only patients 1 and 2 shared the haplotype of A2/B35/Cw3/DR8/DQ1. No other members demonstrated abnormal hematologic findings or shared the above haplotype, although the HLA type was not examined in one individual.

Several reports have suggested a genetic role in the etiology of PV that occurs in families [1,2]. PV appears more commonly in Jews as compared with Caucasians [3]. Regarding HLA antigens, HLA-B52 and HLA-DR7 have been found more frequently in PV patients as compared with normal healthy individuals, whereas HLA-DR4 has been documented less frequently [4]. Alternatively, some cases of familial PV appear to result from frequent exposure to organic solvents [5]. Therefore, genetic and/or environmental factors might be implicated in this disorder.

Neither of our patients was Jewish; nor had they been frequently exposed to organic solvents. They also did not possess either the HLA-B52 or HLA-DR7 antigen. Therefore, the shared haplotype of A2/B35/Cw3/DR8/DQ1 may have been responsible for this familial occurrence of PV. Further examination is necessary to clarify the existence of such a causal relationship.



HLA haplotype a : A2 B35 Cw3 DR8 DQ1
haplotype b : A2 B44 CwBL DR13 DQ1
haplotype c : A24 B55 Cw3 DR2 DQ1
haplotype d : A24 B7 Cw7 DR14 DQ1

Fig. 1. HLA types of family members.

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Intravenous Immune Globulins and Hypothermia

To the Editor: We would like to report on a patient who presented recurrent episodes of hypothermia following intravenous immune globulin (IVIG) infusions. This 58-year-old man had been diagnosed with stage IV B cell chronic lymphocytic leukemia (B-CLL) 15 years earlier. A prophylactic